

CEREBRAL DYSFUNCTION IN CHRONIC ALCOHOLISM

SYMPTOMATOLOGY AND COURSE, RELATED TO
REGIONAL CEREBRAL BLOOD FLOW AND
PSYCHOMETRIC PERFORMANCE

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LUND 1977

Cerebral dysfunction in chronic alcoholism

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AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen

kommer att offentligen försvaras i

Psykiatriska klinikens föreläsningssal

vid Lunds Lasarett

torsdagen den 17 februari 1977 kl. 9⁰⁰

av

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Med. lic. Hb

Lund

1977

Dokumentutgivare
The Department of Psychiatry
University of Lund
Handläggare

Dokumentnamn
Report
Utgivningsdatum
Jan 1977

Dokumentbeteckning
LUMEDW/(MEPL-1012)/
Ärendebeteckning 1-24/(1977)
Academical thesis

Författare
Mats Berglund

Dokumenttitel och undertitel

CEREBRAL DYSFUNCTION IN CHRONIC ALCOHOLISM (5 encls). Symptomatology and course related to regional cerebral blood flow and psychometric performance.

Referat (sammandrag)

Sixty alcoholics including seven with Korsakoff's psychosis were studied with ratings of personality impairment (33 cases), measurements of the regional cerebral blood flow, (^{133}Xe intra-arterial method) and psychometric tests. The examination was repeated about 3.5 years later (no flow measurements). Signs of low vitality correlated to low flow values (organic impairment) and psychometric defects while signs of emotional deficiency and a defence attitude did not. Mean flow decreased with age, possibly due to excessive drinking. Continuous drinkers showed more signs of organic impairment than intermittent drinkers. Alcoholics were less impaired both psychometrically and socially than patients with presenile dementia with similar mean flow levels. Over-all psychometric performance correlated to the prognosis while personality impairment and flow did not. Impaired spatial problem-solving ability was reversible, if the drinking ceased while signs of rigidity and personality impairment were not. The findings suggest that measurements of the cerebral blood flow during activation procedures (such as psychological testing) have greater clinical significance than measurements at rest.

Referat skrivet av
The author

Förslag till ytterligare nyckelord

Klassifikationssystem och -klass(er)

PSYCHIATRY, ALCOHOLISM (Excerpta Medica)

Indextermer (ange källa)

Alcoholism, Korsakoff's syndrome, Regional cerebral blood flow, Psychological tests (Index Medicus)

Omfång
24 pages + 5 encls

Övriga bibliografiska uppgifter

Språk
English

Sekretessuppgifter

ISSN

ISBN

Dokumentet kan erhållas från

The Department of Psychiatry, University
Hospital, s-221 85 Lund, Sweden

Mottagarens uppgifter

Pris

Department of Psychiatry, University Hospital, Lund, Sweden

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CEREBRAL DYSFUNCTION IN CHRONIC ALCOHOLISM

Psychomotor and cognitive, related to
regional cerebral blood flow and
psychometric performance

Marie Permand



June 1975

The present thesis is based upon the following papers

I. M. BERGLUND and D.H. INGVAR

Cerebral blood flow and its regional distribution in alcoholism and in Korsakoff's psychosis.

J. Stud. Alc. 37: 586-597, 1976.

II. M. BERGLUND and B. SONESSON

Personality impairment in alcoholism. Its relation to regional cerebral blood flow and psychometric performance.

J. Stud. Alc. 37: 298-310, 1976.

III. M. BERGLUND and H. LEIJONQVIST

Health insurance records of chronic alcoholics. A study of the prediction of cerebral dysfunction.

J. Stud. Alc. Submitted for publication 1976.

IV. M. BERGLUND, H. LEIJONQVIST and M. HÖRLEN

The prognostic significance and reversibility of cerebral dysfunction in alcoholics. A follow-up study.

J. Stud. Alc. Accepted for publication 1976.

V. M. BERGLUND, L. GUSTAFSON, B. HAGBERG, D.H. INGVAR, L. NILSSON, J. RISBERG and B. SONESSON

Alcohol dementia and presenile dementia, a comparison of two groups of patients with similar reduction of the cerebral blood flow.

Acta psychiat. scand. Submitted for publication 1976.

These papers will be referred to by their roman numbers.

ACKNOWLEDGEMENTS

The author is indebted to all members of the staff of the Department of Psychiatry, University Hospital, Lund. Special thanks are given to Prof. Lennart Nilsson for his encouraging advice and aid. I am most grateful to Prof. David H. Ingvar, head of the Department of Clinical Neurophysiology, for his assistance, support and valuable criticism. Many thanks are given to Mrs Bodil Pihlsgård and Miss Eva Skagert for excellent secreterial assistance. Fil. lic. Bengt Sonesson, psychologist Hans Leijonqvist and psychologist Margareta Hörlén are thanked for stimulating collaboration. Dr Ulf Zätterström aided in the initial part of the study. Muriel Larsson, B.A., aided in the English translation. Miss Stina Bengtsson at the County Temperance Board helped with the social information.

The studies were aided by grants from the Swedish Medical Research Council (contract 21X-3950 and a personal grant 61P-4816).

The present thesis concerns the long-term effects of excessive alcohol intake upon the central nervous system. Chronic brain syndromes associated with alcoholism are mainly of two types: 1. A numerically limited group with specific patho-anatomical changes, the Wernicke-Korsakoff syndrome (DELAY and BRION 1969, VICTOR et al. 1971) and 2. a large group lacking specific patho-anatomical changes and with only moderate unspecific ones, sometimes called 'alcohol dementia'. In this thesis the emphasis will be on 'alcohol dementia'.

In non-Korsakoff alcoholics, disseminated degenerative histopathological changes in the brain especially in the frontal lobes have been reported (COURVILLE 1955, LYNCH 1960). In addition, pneumoencephalographic studies have shown that cerebral atrophy is more prevalent in alcoholics than in non-alcoholics (HAUG 1968), the amount of atrophy correlated to memory deficits and other signs of intellectual deterioration (FERRER et al. 1970, BREWER and PERRETT 1971, CARLSSON et al. 1970). A recent study with computerised axial tomography has shown a high prevalence of cerebral atrophy in alcoholics (MYRHED et al. 1976).

The functional activity level of the brain in chronic alcoholism also seems to be affected. The cerebral blood flow level is reduced (BATTEY et al. 1953, INGVAR et al. 1969, HEISS et al. 1974) indicating a reduced metabolism (RAICHLE et al. 1975). Electroencephalographic studies have shown an increased frequency of abnormalities (FUNKHOUSER et al. 1953, DELAY et al. 1957).

Psychometric studies have shown two general areas of deficit. One involves abstract reasoning and problem solving, the other complex perceptual-motor functions (c.f. KLEINKNECHT and GOLDSTEIN 1972).

A great number of studies have dealt with the diagnosis of cerebral dysfunction in alcoholics while only a few investigators have related the cerebral dysfunction to the clinical characteristics

and the course of the alcoholism. The clinical importance of cerebral dysfunction in alcoholics is thus still incompletely understood.

There is, however, evidence that the personality impairment of chronic alcoholics is related to signs of atrophy in the pneumoencephalogram (CARLSSON and NORDSTRÖM 1964) and to organic psychometric impairment (BOEKE 1970). Furthermore the drinking pattern seems to be of importance. It has been reported that alcoholics who could drink continuously without social complications often develop signs of cerebral dysfunction (BREWER and PERRETT 1971).

The degree of cerebral dysfunction does not influence the prognosis according to two studies of moderately impaired alcoholics (GOLDSTEIN 1972, MCLACHLAN and LEVINSON 1974). A considerable reversibility of the cerebral dysfunction in alcoholism measured with psychometric tests has also been reported after long-term abstinence (MCLACHLAN and LEVINSON 1974, LONG and MCLACHLAN 1974).

In conclusion, there is some strong evidence that chronic alcoholics have a moderate and mainly diffuse cerebral atrophy with preponderance in the frontal lobes. The clinical significance of this atrophy is, however, not very well understood and there are even indications that a moderate degree of cerebral dysfunction i.e. 'alcohol dementia' does not influence the future course. In the present study attention was therefore paid both to the measurements of cerebral dysfunction and to the relation between this cerebral dysfunction and the clinical characteristics and the future course of the alcoholics studied.

The principal aims of the present thesis were:

- I. To study the cerebral blood flow and its regional distribution in chronic alcoholism and in Korsakoff's psychosis.

- II. To study the personality impairment in alcoholism and its relation to regional cerebral blood flow and psychometric performance.
- III. To predict the degree of cerebral dysfunction in chronic alcoholism by means of the Health Insurance Records.
- IV. To study the prognostic significance and the reversibility of cerebral dysfunction in alcoholics.
- V. To compare alcoholics and preseniles with similar reduction of the cerebral blood flow.

MATERIAL

The patient group.

The sample of chronic alcoholics consisted of 7 patients with Korsakoff's psychosis and 53 patients without. For ethical reasons only alcoholics who according to clinical judgement could benefit from the examination were included. The present group of alcoholics thus comprised patients with severe abuse in which brain damage was suspected.

The Korsakoff group consisted of 4 males and 3 females with an average age of 45 ± 12 years at the first examination. This group was analysed in paper I and III. The non-Korsakoff group consisted only of males with an average age of 45 ± 10 years. This group consisted further of an earlier series of 22 patients who were analysed in paper I, III, IV and V and a later series of 31 patients who were used in all papers. Only the later series was rated regarding personality impairment at the initial examination.

All patients were volunteer admissions. They showed at least two of the three cardinal symptoms of alcoholism (KALIN 1960): a) an abnormal craving for more alcohol after ingestion of small quantities; b) regular occurrence of blackouts following ingestion; and c) a physical dependence on alcohol, indicated by withdrawal symptoms after drinking is stopped.

The patients had a history of excessive alcohol use ranging from 5 to 40 years. They were all 'pure' alcoholics and had no history of drug abuse. Sixteen of the patients had had delirium tremens and 15 had epileptic seizures during withdrawal periods.

The patients were generally in good physical health. However, 2 patients had hepatic cirrhosis and 3 a moderate arterial hypertension. One had a mild diabetes without complications and one some respiratory insufficiency.

The psychometric control group.

The control group consisted of 21 male psychiatric in-patients with a mean age of 40 ± 8 years and 11 men from a re-training school with a mean age of 41 ± 8 years. No patients with earlier alcoholic problems, with any kind of suspected brain damage, with any suspected psychotic disorder or with a serious physical disorder were included. No patient had been treated with ECT (electroconvulsive therapy). 19 had only a primary school education and 13 high school or higher levels. There were no differences in the psychometric performance between the psychiatric patients and the re-training school pupils.

METHODS

The psychiatric rating scales.

A rating instrument was constructed to record different signs of personality impairment which could be observed directly during the psychiatric interview. Three different "syndromes" of personality impairment were used. The first syndrome (the Defence syndrome) included items related to the intellectual attitude of the alcoholic towards his drinking, corresponding to the rationalization system (JELLINEK 1946). The second syndrome scale included signs of Emotional deficiency, which are often reported in alcoholics (c.f. KAIJ 1960). The third syndrome was labelled the Low-Vitality syndrome and was close to SJÖBRING's (1958, 1973) description of the

chalarophrenic syndrome with its decreased basic muscular tension and low level of mental intensity. The items of the three syndrome scales are given below. All items were scored as absent or present.

A: The Defence Syndrome.

1. Indifference in contact
2. Guarded attitude
3. Rejecting attitude
4. Disparagement,
rationalization

Although the patients had been admitted voluntarily many had intellectual or emotional inhibitions in talking about their alcohol problems. They were indifferent in their contact with the investigator when the alcohol problem was discussed, pretending it was nothing to talk about or to seek advice for. However, when the investigator continued to discuss it, some patients started to speak openly, but others continued to show a guarded attitude throughout the interview and rejected the topic actively on and off. Many patients also used disparagement and rationalization of their alcohol problem.

B: The Low-Vitality Syndrome.

1. Low mental intensity
2. Flaccidity of movements
3. Bloated and flaccid features
4. Immobility of facial expression

Some patients had a low mental intensity. They also showed flaccidity of movements, bloated and flaccid features and immobility of facial expression.

C: The Emotional-Deficiency Syndrome.

1. Affective bluntness
2. Shallow and poor affective reactions

Some patients showed an affective bluntness, sometimes with affective strength, or they demonstrated only shallow and poor affective reactions.

- | | |
|-----------------------------------|---|
| 3. Euphoria | Some were <u>euphoric</u> without apparent |
| 4. Slow emotional reactions | reason. The patients sometimes showed |
| 5. Emotional rigidity | <u>slow emotional reactions</u> when the |
| 6. Stereotyped emotional response | emotional atmosphere changed. Their |
| 7. Circumstantiality | responses were further characterized |
| 8. General indifference | by <u>emotional rigidity</u> or, in some |
| | pronounced cases, by a <u>stereotyped</u> |
| | <u>emotional response</u> . Some showed a |
| | pronounced <u>circumstantiality</u> and talk- |
| | ed a lot about irrelevant topics. So- |
| | me patients finally had a <u>general in-</u> |
| | <u>difference</u> concerning their general |
| | life situation. |

The scales were analysed for homogeneity by means of a modified Likert analysis (SMITH and MARKE 1958). It was found that the three scales were homogeneous with all items accepted.

Prior to the main investigation 11 alcoholics were rated simultaneously by means of the present scales by the author and another psychiatrist who had a long clinical experience of treatment of alcoholics. The ratings were compared after each patient. Since so few patients were studied it was not considered appropriate to calculate the interjudge reliability statistically. However, in the last examined 6 patients the raters scored equal in 73 of 96 ratings.

The rCBF technique.

The measurement of rCBF was made by means of the intra-arterial ¹³³Xenon method. In the first 22 patients an 8-detector and in the subsequent 38 patients a 32-detector arrangement was used. For comparison the 32-detector studies were transformed into an 8-detector pattern. The computer-operated multidetector equipment has been described in detail elsewhere (INGVAR and GUSTAFSON 1970, SVEINSDOTTIR et al. 1971, LASSEN and INGVAR 1972). Regional values for the following rCBF parameters were calculated.

- f_{10} : calculated according to the height-over-area principle from the first 10 minutes of the clearance curve
- f_g : calculated from the fast component obtained by bi-exponential analysis of the clearance curve, representing the flow in the grey matter
- f_w : calculated from the slow phase obtained in the bi-exponential analysis of the clearance curve, representing the flow mainly in the white matter
- g% : the relative weight of the grey matter calculated from the bi-exponential analysis of the clearance curve from the intercepts at time zero for the fast and slow components.

The psychometric instruments.

The following instruments were used. The last three tests were only given to the late series of 31 patients. The first nine tests were given to the control group.

1. The Standard Progressive Matrices (RAVEN 1960)
2. The USTM Synonym Test (PRIEN 1957)
3. The Paired Associates (CRONHOLM and MOLANDER 1957)
4. The Block Design (KOHS 1971)
5. The Memory for Design (GRAHAM and KENDALL 1960)
6. The Mirror Test (SMITH 1952)
7. The Serial Color Word Test (KRAGH and SMITH 1972)
8. The Visual Retention Test (BENTON 1963)
9. The Psychomotor Reaction Time Test (The Department of Clinical Psychology, Lund 1974)
10. The Tests of Fine Motor Abilities (CRAWFORD and CRAWFORD 1956)

RESULTS

The cerebral blood flow and its regional distribution in alcoholism and in Korsakoff's psychosis (I)

The Korsakoff and non-Korsakoff alcoholic groups were compared regarding the different regional cerebral blood flow, rCBF, parameters with seven healthy young men examined at the same laboratory by INGVAR *et al.* 1965. It was found that the non-Korsakoff alcoholics had lower mean hemispheric grey, f_g , and white matter flow, f_w , than the healthy controls. The Korsakoff group had as a group mean hemispheric rCBF values similar to the healthy controls but the intra group variations were large. The non-Korsakoff alcoholics had lower mean hemispheric ten minutes flow, f_{10} , and grey matter flow than the Korsakoff group.

There was further a successive fall with age of the f_{10} , ($r = 0.40$) and f_g ($r = 0.32$) parameters in the non-Korsakoff alcoholic group. There were however no differences in the rCBF results between alcoholics of the same chronological age but with differences in the length of excessive drinking. There were further no differences between typical gamma alcoholics with heavy benders (JELLINEK 1960) and the others or between alcoholics with previous delirium tremens or abstinence epilepsy and the others.

The chronologically oldest alcoholics (median cut) were compared with the youngest regarding the regional distribution. It was found that the older alcoholics had a relatively lower flow in the anterior temporal region regarding f_{10} , f_g and $g\%$ than the younger alcoholics. Further in the lower frontal region f_{10} was proportionally more reduced in the older group. In the Korsakoff group there was no marked flow reduction in the temporal region.

The main finding in this paper was the successive fall of the mean hemisphere rCBF parameters with age. We do **not know** to what extent this reduction differs from that found in a non-alcoholic population

of corresponding age. There are at present no studies of elderly subjects who have been measured with the intraarterial rCBF technique. However, the healthy subjects studied by DASTUR et al. (1963) and by LASSEN et al. (1960) as well as the old schizophrenics studied by INGVAR and FRANZEN (1974) showed that the cerebral blood flow, CBF, does not fall significantly with increasing age in subjects who have not been exposed to organic brain diseases. This would appear to support the conclusion that the flow reduction in the alcoholics with increasing age which we found was not caused by age per se, but could possibly have been caused by excessive drinking, directly or indirectly. Since CBF is ultimately regulated by the oxidative metabolism of the neurons (INGVAR and LASSEN 1975) the flow reduction which we have demonstrated most likely represents a reduction of the cerebral metabolism.

Concerning the regional distribution of the cerebral blood flow, the reduction found in the anterior temporal region in the oldest alcoholics was of the same magnitude as that in the least impaired groups of presenile patients (showing a selective memory deficit) studied by HAGBERG and INGVAR (1976). In addition there was a low f_{10} in the lower frontal region, resulting in a flow pattern that differed from the one found in the preseniles. As mentioned above several studies have demonstrated a predominance of pathoanatomical changes as well as of pneumoencephalographic signs of atrophy in the frontal region in alcoholics.

Personality impairment in alcoholism and its relation to regional cerebral blood flow and psychometric performance (II).

The extreme groups with many and few symptoms, respectively (cuts as close to the upper and lower quartiles as possible) in each of the three 'syndromes', the Defence, the Low Vitality and the Emotional Deficiency were compared with regard to the regional cerebral blood flow and the psychometric performance.

The group with many symptoms of Low vitality had a poorer performance in the immediate reproduction and retention in the Paired Associates and in the pin part of the Fine Motor Abilities test compared with the group with no symptoms. The first group had also more errors of the memory type in the Visual Retention test and a longer first reading time in the Color Word test. This group with many symptoms of Low Vitality had also a tendency (not significant) to lower f_{10} , and f_g flows compared with the group with no symptoms.

There were no differences between the extreme groups of the Defence and Emotional Deficiency syndromes either in the psychometric performance or in the mean cerebral blood flow parameters.

The Low Vitality syndrome is very similar to the syndrome "chalarophrenia" described by SJÖBRING (1958, 1973). This later syndrome is characterized by a decreased basic muscular tension and mental symptoms of fatigue, defective power of concentration and low level of mental intensity. In patients with this syndrome NYMAN (1952) and NILSSON (1960) found a lower electroencephalographic frequency, indicating a reduced cerebral metabolism and NILSSON and SMITH (1962) showed a consistent but defective adaptive style by several psychometric tests. SJÖBRING was of the opinion that "chalarophrenia" was caused by different, unspecific cerebral lesions.

The present results further indicate that signs of Defence and Emotional Deficiency are not related to cerebral dysfunction. The psychological and social factors concomitant with the addiction therefore probably are of main importance for development of these syndromes.

The prediction of cerebral dysfunction by means of the Health Insurance Records (III).

48 alcoholics including 6 patients with Korsakoff's psychosis were used in this study of the Health Insurance Records. 12 patients were

excluded, 3 because they had a disablement pension at the time of the examination, 5 because they were selfemployed and had different insurance conditions which were not comparable, 3 because their insurance card could not be found and one Korsakoff patient in whom the onset of the psychosis could not be determined. The diagnoses were divided into two categories, mental disorders and physical disorders. In each group, two different parameters were used: the total number of days of illness (disability rate) and the total number of periods of illness (frequency rate) both calculated over a period of five years before the examination, or in the Korsakoff group before the onset of the psychosis. A median cut was done in each of the different parameters and the high and low scoring groups were compared. The Korsakoff group was treated separately.

There was almost zero correlation for the disability and frequency rates of mental disorders compared with the rates of physical disorders. It was further found that only the frequency rate of mental disorders had a discriminatory power regarding cerebral dysfunction. Those who had a low frequency rate of mental disorders had more signs of cerebral dysfunction in the psychiatric ratings and in the psychometric tests. On the other hand, those who had a high frequency rate of mental disorders were less stable in their jobs, were more often divorced and had previously more often been treated at psychiatric wards and committed to institutions for alcoholics. They reported also more often of blackouts and a total neglect of food during drinking bouts.

It was further found that the Korsakoff group had a lower frequency rate of mental disorders before their psychosis than the other alcoholics. This supports the validity of the finding reported above.

The present findings are in agreement with some previous reports. BREWER and PERRETT (1971) found that socially stable alcoholics often have signs of cerebral dysfunction. BJURULF et al. (1971) found a relation between social stability and hepatic cirrhosis in alcoholics.

The important underlying variable is probably the drinking pattern. It is possible that the alcoholics who had a low frequency rate of mental disorders manage to drink continuously during long periods without social complications unlike the other alcoholics. It therefore seems to be the better controlled alcoholics, both socially and as to drinking behaviour, who more often have signs of brain dysfunction.

The prognostic significance and reversibility of cerebral dysfunction in alcoholics (IV).

The non-Korsakoff alcoholic group was reexamined 3.7 ± 1.2 years after the first examination. The clinical ratings and the psychometric examination were performed in 40 patients. One patient refused psychometric examination and one also the interview. Two were drunk at all contacts during the follow-up period, two could not be traced for a personal interview, two were handicapped by physical disorders and five had died including two who had committed suicide. All were examined in a sober state without any signs of withdrawal.

The alcoholics were judged as improved or unimproved according to the drinking pattern during the follow-up period.

17 were regarded as improved and 31 as unimproved. The 2 patients who were handicapped by physical disorders and the 3 patients who were diseased by disorders not directly related to the alcoholism were not included in this judgement. Among the patients who were examined 14 were improved and 26 were unimproved.

The psychometric results of the first examination were compared with a male control group of similar age. The alcoholics were significantly impaired in six tests, namely the Block Design, the deviation from expected retention in the Paired Associates, the difference from expected number of errors in the Visual Retention test, the first reading of the Color word test and the initial time and total time of the Mirror test.

An index of impairment was calculated using these six tests with the exception that the verbal intellectual level minus the Block level was used instead of the Block level. One standard deviation below the mean results of the control group was regarded as impaired. The number of impaired tests divided by the total number of tests performed was used as an index of impairment.

It was found that a large number of impaired tests was associated with a poorer prognosis ($p < 0.05$). Only 35 % of the improved group was impaired in more than two sixths of the tests compared with 58 % of the unimproved group. Further, only 12 % of the improved group was impaired in more than half of the tests compared with 32 % of the unimproved group. The performance of the single psychometric test or the scores of the psychiatric ratings (only performed in the later series of 31 alcoholics) were not significantly associated with the prognosis.

When the reversibility of the impaired psychometric performance was studied it was found that the improved alcoholics ameliorated more than the unimproved in the Block test. In the Color Word test there were no differences of the amelioration between the two groups. In the memory tests there was a tendency (not significant) for the improved group to ameliorate more than the unimproved one.

Regarding the ratings of the personality impairment (only in the later series of alcoholics) it was found that there was a general improvement in the Defence syndrome in the total group of alcoholics. In the Low Vitality and Emotional Deficiency syndromes there was, however, no amelioration of the scores in any of the two alcoholic groups. There was, however, a tendency (not significant) that the unimproved group deteriorated in the Low Vitality syndrome.

The unimproved alcoholics who deteriorated in the Low Vitality syndrome showed more impairment in the Block test than the unimproved alcoholics who did not deteriorate. In the Defence and Emotional Deficiency syndrome there were no such tendencies.

On the other hand, lower score in the Defence and Emotional Deficiency syndrome of the second examination compared with the first one were related to a report of an increased self-esteem. No such tendency was found in the Low Vitality syndrome.

Alcoholics who improved their drinking habits were less psychometrically impaired at the first examination than those who did not improve their drinking. This association, however, was not very strong. It was significant at the 5 % level and found only in the overall performance. There is therefore no reason for therapeutic nihilism in cases with moderately impaired psychometric performance.

The psychometrically impaired abilities showed varying capacity for reversibility. The spatial problem-solving ability showed a good reversibility while the rigidity and adaptive inability hardly changed at all.

The present finding of a relation between changes in the Low Vitality score and changes in the Block performance supports the finding in paper II of an organic origin of the Low Vitality syndrome.

The lack of such a relation in the Defence syndrome and in the Emotional Deficiency syndrome and the relation between changes in these syndromes and changes in self-esteem supports the suggestion in paper II that these two syndromes were mainly related to the psychological and social factors concomitant to the addiction.

A comparison of alcoholics and preseniles with similar reduction of the cerebral blood flow (V).

It was possible to match in pairs 15 non-Korsakoff alcoholics from the present series (those with the lowest flows) and 15 preseniles from the series described by GUSTAFSON and RISBERG (1974) with regard to the mean rCBF level (f_{10} , f_g and $g\%$). The matching did not take age or sex into account. The age of the alcoholics were 46 ± 10 years and that of the preseniles 56 ± 10 years.

It was found that there were no significant differences in the regional distribution or in the mean f_w . The performance of the preseniles, however, was much poorer than that of the alcoholics on all the tests. Furthermore, 12 of the alcoholics were still employed and working compared with only 3 of the 11 preseniles who had previously been employed. None of the alcoholics compared with 8 of the preseniles had to have a constant supervision at home or institution. Six of the presenile patients had neurological deficits which could influence the social performance.

It has been convincingly proved (i.e. RAICHLE et al. 1975) that rCBF parameters mirror the level of the functional activity in the brain. There is therefore reason to believe that the metabolic functional level of the brain was similar in the present two groups of alcoholics and preseniles.

The rCBF measurements were made at rest while the psychometric studies and the social performance give information about the working brain. The difference found in the present study perhaps could indicate that alcoholics could more effectively activate their brains, in test situations and socially, than the preseniles. Evidence to support this view is obtained in activation studies of preseniles who showed less rCBF changes than normals (INGVAR, RISBERG and SCHWARTZ 1975). Furthermore, it has been shown that rCBF measured at rest is related to the general degree and regional distribution of cortical atrophy in presenile dementia except in cases of brain stem lesions, where the relation is more dubious (BRUN et al. 1975, GUSTAFSON et al. 1976). In the present study signs of brain stem dysfunction were indeed more common in the preseniles than in the alcoholics. Therefore it appears likely that the alcoholics performed better because they could more effectively activate the brain in social and test situations.

This view is supported by the finding of RISBERG and INGVAR (1973) who studied rCBF during the psychometric performance in 15 alcoholics

(a part of the present total material of chronic alcoholics) and of INGVAR, RISBERG and SCHWARTZ (1975) who did the same in 25 preseniles (of the present larger series of preseniles). The mean flow level of the alcoholics was somewhat higher than in the present series ($f_{10} = 45 \pm 4$, $f_g = 68 \pm 11$, $g\% = 49 \pm 4$) and the level of the preseniles somewhat lower ($f_{10} = 36 \pm 6$, $f_g = 54 \pm 9$, $g\% = 46 \pm 5$). The alcoholics increased their blood flow with 7 % (f_{10}) and 13 % (f_g), respectively, while the preseniles did not increase the f_{10} flow and increased their f_g flow with only 7 %.

GENERAL COMMENTS

The regional cerebral blood flow, rCBF, technique.

The presently used rCBF technique necessitates an intra-carotid injection. The risk for complications related to this injection is low, almost nil in patients without evidence of gross intra-cranial or cerebrovascular disease (INGVAR and LASSEN 1973). Patients with chronic alcoholism as a rule belong to this group. These complications of the injection can today be eliminated by the newly developed Xe^{133} inhalation method (OBRIST *et al.* 1975, RISBERG *et al.* 1975). The inhalation method makes it possible to study both hemispheres at the same time but has also some disadvantages. Only the grey matter flow can be measured and the regional resolution is lower than with the intra-carotid technique.

RCBF and chronic alcoholism.

The main rCBF findings in the present study were the decrease of the cerebral blood flow with age, which possibly was caused by the excessive drinking directly or indirectly. Since the cerebral blood flow is regulated by the oxidative metabolism of the neurons, this finding represents a reduction of the cerebral metabolism. Previous patho-anatomical and pneumoencephalographic studies cited in the introduction have shown an increased loss of neurons in chronic alcoholism and a reduction of the number of neurons means a reduction of the cerebral metabolism. One explanation to the decreased cerebral blood flow is probably loss of neurons.

This rCBF finding in alcoholics could, however, not solely be explained by loss of neurons. The main objection is the results of the comparison between alcoholics and presenile patients with similar cerebral blood flow levels. The alcoholic group performed much better both psychometrically and socially than the presenile group.

It has been shown that subsymptoms of presenile dementia correspond to regional reductions of the cerebral flow as well as to regional degenerative pathoanatomical changes (BRUN, GUSTAFSON and INGVAR 1975, HAGBERG and INGVAR 1975, GUSTAFSON, BRUN and INGVAR 1976). Thus in alcoholics probably both a reduction of neurons and a reversible component explain the rCBF reduction.

The present alcoholic series was examined when the withdrawal period had passed. It was further found that some of the impaired psychometric performances at the first examination improved at the follow-up examination some years later if the drinking habits had considerably improved. Thus there seems to be a long-term reversibility of the cerebral dysfunction in alcoholics. This finding seems to be consistent with the description on an "intermediate stage of alcoholic brain syndrome" made by BENNETT et al. (1960). These investigators based their description on EEG findings in 227 examined cases of alcoholism. They were of the opinion that this reversible intermediate stage had a duration of a couple of months.

Perhaps this intermediate stage of cerebral dysfunction in alcoholics corresponds to a cerebral blood flow pattern with low resting values but normal activation patterns i.e. the findings in the present alcoholic group which was compared to a presenile dementia group. This problem requires further studies.

RCBF, the clinical characteristics and the course of the alcoholism.

It was not possible to demonstrate a significant relationship between the reduction of the cerebral blood flow and the clinical characteristics on the course of the alcoholism. There was however a relation-

ship (n.s.) between symptoms of Low vitality and a reduction of the cerebral blood flow. This relation is in accordance with a study by NILSSON (1960) who showed that symptoms of flaccidity were associated with lowered EEG frequencies in a series of psychiatric patients.

Impairment in psychometric performance on the other hand was related to a worse course, to a continuous drinking pattern and many symptoms of Low vitality. One of the probable reasons for this discrepancy is that the rCBF was measured on the resting brain while the psychometric performance means measurement of the activated brain. Brain activation studies thus possibly give results of a higher clinical significance than studies of the brain at rest. The present study did not include measurements of rCBF during activation (testing) which could be correlated with the psychometric findings, the clinical characteristics and the course. These correlations will thus require further studies.

The connection between alcohol and cerebral dysfunction.

The present study showed that continuous drinkers more often than intermittent drinkers developed signs of cerebral dysfunction. This is in accordance with previous studies, both of cerebral and hepatic dysfunction (BREWER and PERRETT 1971, BJURULF, STERNBY and WISTEDT 1971). Whether alcohol influences the brain directly or indirectly could not be answered with certainty in the present study. However, none of our results precludes a direct effect of alcohol on the brain even if there is no positive indications for this direct mechanism. The different possibilities for an indirect mechanism are, however, less likely a) A nutritional mechanism because the alcoholics with the most pronounced brain dysfunction reported a better food intake during drinking periods than the other alcoholics b) Repeated head injuries because there was no relation between reported brain concussions and reduction of the rCBF, impairment of the psychometric tests and many symptoms of personality impairment c) Hepatic dysfunction because the great majority of the patients had no such signs.

GENERAL CONCLUSION

The clinical implications of the present study thus are:

1. The degree of cerebral dysfunction measured with psychometric testing is associated with the future course in chronic alcoholism.
2. It appears likely that the cerebral dysfunction demonstrated in the present alcoholics, who had psychometric defects and a low cerebral blood flow level, consists of two components. One is probably related to the loss of neurons and the other which partly could be overcome by activation procedures is reversible to judge from our follow-up data.
3. It is suggested to use activation procedures in future studies for measuring cerebral dysfunction. In the present study psychometric testing which implies activation of the brain yields clinical significant information about symptomatology and future course in contrast to the measurements of the cerebral blood flow which gives information about the brain at rest.

REFERENCES

- BATTEY, L. L., HEYMAN, A. and PATTERSON JR., J.L. (1953) Effects of ethyl alcohol on cerebral blood flow and metabolism. *J. Amer. med. Ass.* 152: 6-10.
- BENNETT, A.E., MOWERY, G.L. and FORT, J.T. (1960) Brain damage from chronic alcoholism: The diagnosis of intermediate stage of alcoholic brain disease. *Am. J. Psychiat.* 116: 705-711.
- BENTON, A.L. (1963) The Benton visual retention test. Rev. ed. New York; Psychological Corporation.
- BJURULF, P., STERNBY, N.H. and WISTEDT, B. (1971) Definitions of alcoholism. Relevance of liver disease and Temperance Board Registrations in Sweden. *Quart. J. Stud. Alc.* 32: 393-405.
- BOEKE, P.E. (1970) Some remarks about alcohol-dementia in clinically-treated alcoholics. *Brit. J. Addict.* 65: 173-180.

- BREWER, C. and PERRETT, L. (1971) Brain damage due to alcohol consumption; an air-encephalographic, psychometric and electroencephalographic study. *Brit. J. Addict.* 66: 170-182.
- BRUN, A., GUSTAFSON, L. and INGVAR, D.H. (1975) Neuropathological findings related to neuropsychiatric symptoms and regional cerebral blood flow in presenile dementia. *Proceedings of VII International Congress of Neuropathology, Budapest.*
- CARLSSON, C., CLAESON, L.-E., KARLSSON, K.-I. and PETTERSSON, L. (1970) Brain damage in chronic alcoholism. *Acta psychiat. scand.*, Suppl. No. 217: 57-58.
- CARLSSON, B. and NORDSTRÖM, E. (1964) Symptoms of cerebral lesion and radiological cerebral atrophy. *Acta psychiat. scand.*, Suppl. No. 180: 105-110.
- COURVILLE, C.B. (1955) *Effects of alcohol on the nervous system of man.* Los Angeles; San Lucas Press.
- CRAWFORD, J.E. and CRAWFORD, D.M. (1956) *The Crawford Small Parts Dexterity Test.* New York; Psychological Corporation.
- CRONHOLM, B. and MOLANDER, L. (1957) Memory disturbances after electroconvulsivetherapy. *Acta psychiat. neurol.* 32: 280-306.
- DASTUR, D.K., LANE, M.H., HANSEN, D.B., KETY, S.S., BUTLER, R.N., PERLIN, S. and SOKOLOFF, L. (1963) Effects of aging on cerebral circulation and metabolism in man. In: *U.S. NATIONAL INSTITUTE OF MENTAL HEALTH. Human aging.* (Public Health Service Publ. No. 986) Washington, D.C; U.S. Govt. Print. Off.
- DELAY, J. and BRION, S. (1969) *Le syndrome de Korsakoff.* Paris; Masson.
- DELAY, J., VERDEAUX, J. and CHANOIT, P. (1957) The electroencephalogram of chronic alcoholics. Statistical study. *Ann. Med.-Psychol.* 155²: 427-440 (abstr. *Quart. J. Stud. Alc.* 21: 157, 1960).
- DEPARTMENT OF CLINICAL PSYCHOLOGY, University Hospital, Lund, Sweden (1974) Psychomotor reaction time test, standardized at the Dept.
- FERRER, S., SANTIBÁÑEZ, I., CASTRO, M., KRAUSKOPF, D. and SAINT-JEAN, H. (1970) Permanent neurological complications of alcoholism. In: *POPHAM, R.E., ed. Alcohol and alcoholism; papers presented at the International Symposium in memory of E.M. Jellinek, Santiago, Chile.* Toronto; University of Toronto Press.

- FUNKHOUSER, J.B., NAGLER, B. and WALKE, N.D. (1953) The electroencephalogram of chronic alcoholism. *Southern Med. J.* 46: 423-428.
- GOLDSTEIN, G. (1972) Brain damage as a factor in treatment outcome of chronic alcohol patients. Presented at the meeting of the American Psychological Association, Miami Beach. (cf. KLEIN-KNECHT, R.A. and GOLDSTEIN, S.G. Neurophysiological deficits associated with alcoholism. A review and discussion. *Quart. J. Stud. Alc.* 33: 999-1017, 1972).
- GRAHAM, F.K. and KENDALL, B.S. (1960) Memory-for-Design Test; revised general manual. *Percept. Motor Skills* 11: 147-188.
- GUSTAFSON, L., BRUN, A. and INGVAR, D.H. (1976) Presenile dementia: clinical symptoms, pathoanatomical findings and cerebral blood flow. 8th Satzburg Conference 1976. To be published.
- GUSTAFSON, L. and RISBERG, J. (1974) Regional cerebral blood flow related to psychiatric symptoms in dementia with onset in the presenile period. *Acta psychiat. scand.* 50: 516-538.
- HAGBERG, B. and INGVAR, D.H. (1976) Cognitive reduction in presenile dementia related to regional abnormalities of the cerebral blood flow. *Brit. J. Psychiat.* 128: 209-222.
- HAUG, J.O. (1968) Pneumoencephalographic evidence of brain damage in chronic alcoholics; a preliminary report. *Acta psychiat. scand.* Suppl. No. 203, pp. 135-143.
- HEISS, W.-D., KÜFFERLE, B. and DEMEL, I. (1974) Störungen der Hirndurchblutung bei chronischen Alkoholikern in Abhängigkeit vom klinischen Bild. *Psychiatria clin.* 7: 181-191.
- INGVAR, D.H., CRONQVIST, S., EKBERG, R., RISBERG, J. and HØEDT-RASMUSSEN, K. (1965) Normal values of regional cerebral blood flow in man, including flow and weight estimates of grey and white matter. *Acta neurol. scand.*, Suppl. 14: 72-78.
- INGVAR, D.H. and FRANZEN, G. (1974) Abnormalities of regional cerebral blood flow in patients with mental deterioration due to chronic schizophrenia. *Acta psychiat. scand.* 50: 425-462.
- INGVAR, D.H. and GUSTAFSON, L. (1970) Regional cerebral blood flow in organic dementia with early onset. *Acta neurol. scand.* 46 (Suppl. 43): 42-73.

- INGVAR, D.H. and LASSEN, N.A., eds. (1975) Brain work; the coupling of function, metabolism and blood flow in the brain. Copenhagen; Munksgaard.
- INGVAR, D.H. and LASSEN, N.A. (1973) Cerebral complications following measurements of regional cerebral blood flow (rCBF) with the Intraarterial ¹³³Xenon injection method. *Stroke* 4: 658-665.
- INGVAR, D.H., RISBERG, J., CRONQVIST, S., ZÄTTERSTRÖM, U., GUSTAFSON, L. and LJUNGBERG, K. (1969) Regional cerebral blood flow in chronic alcoholism. In: BROCK, M. et al., ed. Cerebral blood flow; clinical and experimental findings. New York; Springer; pp. 231-234.
- INGVAR, D.H., RISBERG, J. and SCHWARTZ, M.S. (1975) Evidence of subnormal function of association cortex in presenile dementia. *Neurology* 25: 964-974.
- JELLINEK, E.M. (1960) The disease concept of alcoholism. Highland Park, NJ; Hillhouse Press.
- JELLINEK, E.M. (1946) Phases in the drinking history of alcoholics; analysis of a survey conducted by the official organ of Alcoholics Anonymous. *Quart. J. Stud. Alc.* 7: 1-88.
- KAIJ, L. (1960) Alcoholism in twins; studies on the etiology and sequels of abuse of alcohol. Stockholm; Almqvist & Wicksell.
- KLEINKNECHT, R.A. and GOLDSTEIN, S.G. (1972) Neuropsychological deficits associated with alcoholism. A review and discussion. *Quart. J. Stud. Alc.* 33: 999-1019.
- KOHS, S.C. (1971) Kohs' Block-Design Test. In: Manual till DS-batteriet. (Manual of the DS test battery.) Stockholm; Psykologiförlaget; pp. 54-56.
- KRAGH, U. and SMITH, G.J.W. (1972) Percept-genetic Analysis. Lund; Gleerups.
- LASSEN, N.A., FEINBERG, I. and LANE, M.H. (1960) Bilateral studies of cerebral oxygen uptake in young and aged normal subjects and in patients with organic dementia. *J. clin. Invest.* 39: 491-500.
- LASSEN, N.A. and INGVAR, D.H. (1972) Radioisotopic assessment of regional cerebral blood flow. *Progr. nucl. Med.*, Basel; 1: 376-409.

- LONG, J.A. and MCLACHLAN, J.F.C. (1974) Abstract reasoning and perceptual-motor efficiency in alcoholics. Impairment and reversibility. *Quart. J. Stud. Alc.* 35: 1220-1229.
- MCLACHLAN, J.F.C. and LEVINSON, T. (1974) Improvement in WAIS block design performance as a function of recovery from alcoholism. *J. clin. Psychol.* 30: 65-66.
- MYRHED, M., BERGMAN, H., BORG, S., HINDMARSH, T. and IDESTRÖM, C.M. (1976) Datortomografiska fynd vid hjärnundersökning av beroendepatienter. (Findings with computerised axial tomography in addicted patients.) Stockholm; Läkarsällskapetets riksstämma 1976.
- NILSSON, L. (1960) Physiologic and biochemic representation of some psychiatric variables. Academic thesis, University of Lund.
- NILSSON, L. and SMITH, G.J.W. (1962) Dimensions of overt behaviour as represented in EEG and adaptive tests patterns. *Acta psychiat. scand.* 38: 277-301.
- NYMAN, E. (1952) Elektroencefalografi och psykiatri. (Electroencephalography and psychiatry.) *Nord. med.* 48: 1348-1349.
- OBRIST, W.D., THOMPSON, H.K., WANG, H.S. and WILKINSON, W.E. (1975) Regional blood flow estimated by ¹³³Xenon inhalation. *Stroke* 6: 245-256.
- PRIEN, L. (1957) Manual till USTM-provet. (Manual of the USTM-test.) Stockholm; Skand. Testförlaget.
- RAICHLE, M.E., GRUBB JR, R.L., GADO, M.H., EICHLING, J.O. and TER-POGOSSIAN, M.M. (1975) In vivo correlation between regional cerebral blood flow and oxygen utilization in man. In: HARPER, M. *et al.*, ed. Blood flow and metabolism in the brain. Aviemore, Scotland.
- RAVEN, J.C. (1960) Guide to the Standard Progressive Matrices. London; Lewis.
- RISBERG, J., ALI, Z., WILSON, E.M., WILLS, E.L. and HALSEY, J.H. (1975) Regional cerebral blood flow by ¹³³Xenon inhalation. Preliminary evaluation of an initial slope index in patients with unstable flow compartments. *Stroke* 6: 142-148.

- RISBERG, J. and INGVAR, D.H. (1973) Patterns of activation in the grey matter of the dominant hemisphere during memorization and reasoning; a study of regional cerebral blood flow changes during psychological testing in a group of neurologically normal subjects. *Brain* 96: 737-756.
- SJÖBRING, H. (1973) Personality structure and development. *Acta psychiat. scand.*, Suppl. No. 244.
- SJÖBRING, H. (1958) Struktur och utveckling. (Personality structure and development.) Malmö; Gleerups.
- SMITH, G.J.W. (1952) Interpretations of behaviour sequences. *Stud. Psychol. Paedagog.*, Ser alt. 5.
- SMITH, G.J.W. and MARKE, S. (1958) The internal consistency of the Humm-Wadsworth temperament scale. *J. appl. Psychol.* 42: 234.
- SVEINSDOTTIR, E., TORLÖF, P., RISBERG, J., INGVAR, D.H. and LASSEN, N.A. (1971) Calculation of regional cerebral blood flow (rCBF): initial-slope-index compared to height-over-total-area values. In: ROSS RUSSELL, R.W., ed. *Brain and blood flow; proceedings of the 4th international symposium on the regulation of cerebral blood flow*. London; Pitman.
- VICTOR, M., ADAMS, R.D. and COLLINS, G.H. (1971) *The Wernicke-Korsakoff syndrome; a clinical and pathological study of 245 patients, 82 with post-mortem examinations*. Philadelphia; F.A. Davis Company.

